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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,316	10/23/2003	Mu-En Lee	HUV-046.02	8228
58475	7590	10/10/2007		
FOLEY HOAG, LLP PATENT GROUP (w/HUV HNV) 155 SEAPORT BLVD. BOSTON, MA 02210-2600			EXAMINER MACFARLANE, STACEY NEE	
			ART UNIT	PAPER NUMBER
			1649	
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			10/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/693,316	<b>Applicant(s)</b> LEE ET AL.	
	<b>Examiner</b> Stacey MacFarlane	<b>Art Unit</b> 1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1:704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 24 August 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) 7-9, 12-20 and 22-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6, 10-11 and 21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election with traverse of Group II, claims 1-6, 10, 11, and 21 in the reply filed on August 24, 2007 is acknowledged. The traversal is on the ground(s) that it would not place a serious burden upon the Examiner to examine all of the claims. This is not found persuasive because the inventions of Groups I-IX are drawn to methods that are materially distinct and/or have a separate status in the art as shown by their different classification for reasons of record in the Paper mailed April 18, 2007 and thus would require employing different search queries. For purposes of the initial requirement, a serious burden on the examiner may be *prima facie* shown, by appropriate explanation of separate classification, or separate status in the art, or a different field of search as defined in MPEP § 808.02.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 7-9, 12-20 and 22-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 24, 2007.

### ***Claim Objections***

3. Claim 21 is objected to for being dependent from non-elected claims.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-6, 10, 11, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 1 is vague and indefinite in so far as it employs the term "SM22α" as a limitation. This term appears to be novel, and without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: one cannot determine the metes and bounds of "SM22α". Moreover, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "SM22α", an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

7. Claim 1 is vague in its recitation of "the differentiation of vascular smooth muscle cells comprising culturing neural crest cells". Examiner suggest that rephrasing along the lines of "the differentiation of neural crest cells into vascular smooth muscle cells", would clarify the term.

8. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the active steps and conditions required to induce expression of SM22α.

9. Claim 2 is vague and indefinite in its recitation of "immortalized cells". It is unclear if this is the recitation of an active step required for the method, for which the steps are omitted, or if this is indicating the starting materials to be a neural crest cell line. If the intention is that this refers to a cell line, then a deposit of biological materials will be required under the first paragraph of 35 U.S.C. 112. See 37 CFR 1.804(a) and MPEP § 2406.

10. Claims 1 and 10 are incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. The omitted structural cooperative relationship is that between the elements of vascular smooth muscle cells and neural crest cells.

11. Claim 3 is vague and indefinite in its recitation of smooth muscle cell differentiation medium (SMDM) for which there is no explicit definition in the specification (paragraph bridging pages 12 and 13). Thus, the metes and bounds of the claim are unclear.

12. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps required to perform the culturing of cells in complete medium and the order in which the steps are to be performed.

13. Claim 6 is vague and indefinite in its recitation of "chick embryo extract".

14. Claim 10 is vague and indefinite in its recitation of a method of identifying "an agent that modulates which regulates proliferation or migration...". It is unclear what the agent "modulates" and if this is a limitation that is additional to its requirement of

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regulating proliferation or migration. Furthermore, Claim 10 is missing a final step, it is suggested that recitation of an active detection step may be remedial.

15. Claim 11 is vague and indefinite in its recitation of detecting the "presence or absence" as an indication of the ability of the agent to inhibit differentiation. Since the language encompasses both alternatives it is unclear what constitutes an indication of ability.

16. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the active steps required to support the recitations of formulating, identifying and ability.

17. Claim 4 is indefinite for depending from an indefinite claim.

### ***Claim Rejections - 35 USC § 102***

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

19. Claims 1-6, 10, 11 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Anderson et al. US Patent 5,672,499, filed June 7, 1995, cited on the IDS filed January 28, 2005.

Claims are drawn to methods of identifying an agent that regulates proliferation or migration of smooth muscle cells comprising the steps of culturing neural crest cells under culture conditions wherein SM22 $\alpha$  gene expression is induced, contacting the cells with a test agent and measuring the ability of the test agent to inhibit the differentiation of the neural crest cells to smooth muscle cells, wherein the inhibition of differentiation is detected by the presence or absence of smooth muscle cell markers.

The Anderson et al. reference teaches an immortalized neural crest cell line and "methods for assaying the effects of various substances on neural stem cells. Such effects include the differentiation of said cells into neurons, glia or smooth muscle cells" (column 3, lines 23-27) and FIGS. 19 A, B and C demonstrate that smooth muscle cell differentiation is promoted by fetal bovine serum as measured by the detection of the smooth muscle cell markers, smooth muscle antigen (SMA) and desmin. The prior art teaches cells are grown in a chemically defined medium identified as L-15 medium (column 14, line 47), supplemented with chick embryo extract (column 13, lines 47-50).

The instant specification states that agents to be tested can include agents be produced by organisms (e.g. natural products), produced chemically (e.g. small molecules, including peptidomimetics), or produced recombinantly (paragraph 110), thus defining the test agents of the invention to broadly include the fetal bovine serum as taught by the prior art. The instant specification also recites that with respect to the components of the growth medium, "equivalents can be utilized and is not intended to be limited to the exact percentages of components...one skilled in the art would be able to make modifications of the SMDM to support and promote the differentiation of the

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neural crest cells" (paragraph bridging pages 12-13). Lastly, the instant specification lacks an explicit definition of a "pharmaceutical preparation". Accordingly, one of ordinary skill in the art would reasonably recognize the fetal bovine serum or the prior art, which can be administered in vivo, does not lead to toxicity of cells in culture, and comprise one or more agents identified as able to modulate proliferation according to the method, teaches the limitations of Claim 21. Thus, the reference fully anticipates the invention of the instant claims.

### ***Conclusion***

20. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on M,W and ALT. F 6 am to 3 pm, T & R 5:30 am - 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane  
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Art Unit 1649

SNM

  
OLGA N. CHERNYSHEV, PH.D.  
PRIMARY EXAMINER